insofar as it represents anything other than an election of species, as there is no basis here to restrict within claim 1.

Claims 1-20, 25, 26, 28, 32, 34, 27, 29, 30, 31, and 33 have been rejected under the second paragraph of 35 U.S.C. 112 for indefiniteness. Reconsideration of the rejection is respectfully requested.

As suggested by the Examiner, the definitions of W have been amended to clarify that the only possible carbon atoms with open valences are the carbons that are part of the ring. Concerning the criticism of R7, applicants maintain that, to the extent that either of the questioned phrases was not clear to one of ordinary skill in the art, the present specification would provide ample clarification. Since the claims must be read in light of the specification, and since both phrases ("natural or unnatural amino acid" and "azaamino acid or a dipeptide radical ---- reduced to -NH-CH2-") are carefully defined therein, one of ordinary skill in the art would have no trouble determining the metes and bounds of R7. However, if the Examiner prefers, applicants would be willing to import these definitions from the specification into the claim.

Accordingly, withdrawal of the rejection under the second paragraph of 35 U.S.C. 112 is requested.

Claims 1-20, 25, 26, 28, 32, 34, 27, 29, 30, 31, and 33 have been rejected under 35 U.S.C. 103(a) as obvious over Zoller ('008, '293, '594) and CA '540 (DE '944). Reconsideration of the rejection is respectfully requested.

Applicants first wish to clarify for the Examiner that claims 1-20 relate to preparations containing a VLA-4 antagonizing effective amount of a compound of formula I; claims 21-24 are method of use claims concerning uses of the preparations of claim 1; claims 25-34 relate to compounds and preparations having particularly VLA-4 antagonistic activity; and claims 35-38 are directed to kits comprising the preparations and instructions for use in antagonizing VLA-4.

While the prior art's vast genus of possible compounds may encompass some of those presently claimed, the prior art in no way suggests the

pharmaceutical activity claimed herein, i.e., VLA-4 antagonizing activity, and the resulting end treatments. It should be immediately apparent to the Examiner that one of ordinary skill in the art would not have been motivated to use the prior art's compounds for the methods of claims 21-24, without the hindsight benefit of knowing from the present specification that they possess VLA-4 antagonizing activity. The prior art only discloses that these compounds possess fibrinogen receptor antagonistic activity, and the prior art postulates that the compounds might be useful in methods based on the fibrinogen receptor antagonistic activity, including platelet aggregation, thrombosis prevention, inhibition of osteoclast binding, and inhbition of cancer metastases.

These uses are far removed from the presently claimed invention. Instant method claims 21-24 are based on VLA-4 receptor antagonization. The presently claimed uses are in no way suggested or enabled by the prior art's disclosure of fibrinogen receptor antagonistic activity. Therefore, claims 21-24 are allowable over the prior art cited in the instant rejection.

In addition, preparation claims 1-20 are allowable over the cited prior art because they require preparations containing a VLA-4 antagonizing effective amount of the compounds of formula I. While the Examiner has provided an extensive explanation of the genus-species relationship between the compounds of the prior art and the compounds of the instant claims, claims 1-20 are simply not compound claims. They are compositions requiring a VLA-4 antagonizing effective amount of compounds that were not known to have any VLA-4 antagonistic activity. As recently held by the Federal Circuit in *Key Pharmaceuticals v. Hercon Laboratories*, 48 USPQ2d 1911 (Fed. Cir. 1998), a functionally defined efficacy range in a pharmaceutical composition claim can distinguish it over prior art showing the same preparation for another use. Such is the case here, where the prior art does not even hint at the VLA-4 antagonistic activity of the compounds.

Moreover, kit claims 35-38 are allowable over the prior art, as well. These claims require instructions for use in antagonizing VLA-4. Computer software patents are granted on programs embodied in floppy disks on the basis of novelty and unobviousness in the instructions recited in the claims relative to the instructions recited in other programs of the prior art. The same principle mandates allowance of the instant kit claims, since the instructions for use in antagonizing VLA-4 establish novelty over the prior art and since they enable the claimed kits to be used for an entirely new purpose not suggested in the prior art.

Lastly, claims 25-34 relate to a selection of particular compounds having VLA-4 antagonistic activity. The Federal Circuit has recognized again and again (in cases such as *In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994) and *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992)) the unobviousness of selection inventions in the pharmaceutical field, which has prompted the Patent Office to recently begin preparing formal guidelines (63 Fed. Reg. 47000) to assist Examiners in determining patentability in genus-species situations, such as the present situation. In fact, the Federal Circuit has ruled that specific compounds may not even be *prima facie* obvious over vast generic disclosures where such disclosures lack sufficiently similar examples that would lead one of ordinary skill toward selection of the claimed substituents. See *In re Baird*. The bottom line is that a generic reference must be considered as a whole, including the general description, preferred embodiments, working examples, and the pharmaceutical activities disclosed in the working examples. All of these factors in a generic reference must be considered. A rejection may not pick and choose only the parts of the reference that would support a rejection. Such rejections, if permitted, would bring an end to all "selection" inventions and would mean that many, many valuable drugs would go undeveloped, only to lie unrecognized and buried within the vast computer-generated paper disclosures of the prior art.

In the instant case, although the rejection has pointed to a species that is structurally similar, there is no disclosure or suggestion that the change in

structure would provide VLA-4 antagonistic activity. As such, the present situation falls squarely within the holding of *In re Stemniski*, 170 USPQ 343 (CCPA 1971).

Accordingly, withdrawal of the rejection under 35 U.S.C. 103(a) is requested.

In view of the foregoing amendments and remarks, favorable reconsideration and allowance of this application are courteously solicited. In the event that any issues remain, the Examiner is invited to telephone the office of the undersigned with any proposal to expedite prosecution.

Respectfully submitted,

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Date

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